

**What is claimed is:**

1. A method of treating an individual who has cancer comprising the steps of identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis, and subsequently administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor.
2. The method of claim 1 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging.
3. The method of claim 1 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging using <sup>18</sup>fluoro-deoxyglucose.
4. The method of claim 1-3 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 1 mM.
5. The method of claim 1-3 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 0.1 mM.
6. The method of claim 1-3 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 50  $\mu$ M.
7. The method of claim 1-6 wherein said cancer comprises cancer cells that are not dependent on endogenously synthesized fatty acid.
8. The method of claim 1-7 wherein ATP citrate lyase inhibitor is selected from the group consisting of compounds having a structure defined by one of the formulae or examples set forth in U.S. Patent No. 5,447,954 and (-)hydroxycitrate.

9. The method of claim 1-7 wherein said ATP citrate lyase inhibitor is SB-204990 shown in Figure 4.

10. A method of treating an individual identified as having cancer wherein said cancer comprises cells that are not dependent on endogenously synthesized fatty acid, said method  
5 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor.

11. The method of claim 10 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis.

12. The method of claim 11 wherein said cancer is determined to be a cancer with cancer  
10 cells that have a high rate of aerobic glycolysis by PET imaging.

13. The method of claim 12 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging using <sup>18</sup>fluoro-deoxyglucose.

14. The method of claim 10-13 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of a different anti-cancer compound.

15. The method of claim 10-13 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

16. A method of treating an individual identified as having cancer comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater  
20 than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 1 mM.

17. The method of claim 16 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 0.1 mM.

18. The method of claim 16 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 50  $\mu$ M.

19. The method of claims 16-18 wherein said cancer comprises cells that are not  
5 dependent on endogenously synthesized fatty acid.

20. The method of claim 16-19 wherein ATP citrate lyase inhibitor is selected from the group consisting of compounds having a structure defined by one of the formulae or examples set forth in U.S. Patent No. 5,447,954.

21. The method of claim 16-20 wherein said ATP citrate lyase inhibitor is SB-204990  
10 shown in Figure 4.

22. The method of claim 16-21 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis.

23. The method of claim 22 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging.

15 24. The method of claim 22 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging using  $^{18}$ fluoro-deoxyglucose.

25. The method of claim 16-24 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of a different anti-cancer compound.

20 26. The method of claim 16-24 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

27. A method of inducing apoptosis in a cancer cell wherein said cancer comprises cells that are not dependent on endogenously synthesized fatty acid, comprising the step of delivering to said cancer cell an amount of an ATP citrate lyase inhibitor effective to induce apoptosis in said cell.

28. A method of inducing apoptosis in a cancer cell comprising the step of delivering to said cancer cell an amount of an ATP citrate lyase inhibitor effective to induce apoptosis in said cell; wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 1 mM.

5 29. The method of claim 28 wherein said ATP citrate lyase inhibitor effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 0.1 mM.

10 30. The method of claim 29 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 50  $\mu$ M.

31. The method of claim 28-30 wherein said cancer cell is a cancer cell that is not dependent on endogenously synthesized fatty acid.

15 32. The method of claim 28-31 wherein ATP citrate lyase inhibitor is selected from the group consisting of compounds having a structure defined by one of the formulae or examples set forth in U.S. Patent No. 5,447,954

33. The method of claim 28-32 wherein said ATP citrate lyase inhibitor is SB-204990 shown in Figure 4.

20 34. A method of treating an individual identified as having cancer comprising the step of administering to said individual a therapeutically effective amount of a tricarboxylate transporter inhibitor.

35. The method of claims 34 wherein said cancer comprises cells that are not dependent on endogenously synthesized fatty acid.

25 36. The method of claim 34-35 wherein said tricarboxylate transporter inhibitor is selected from the group consisting of: 1,2,3-benzenetricarboxylate, isocitrate, malate, phosphoenolpyruvate, n-butylmalonate, sulfhydryl reagents, diethyl pyrocarbonate, 2,3-

butanedione, phenylglyoxal, pyridoxal, 5-phosphate dicarboxylates, succinate, malate, oxaloacetate, tricarboxylates isocitrate, tricarballylate and palmitoyl-CoA.

37. The method of claim 34-36 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis.

5 38. The method of claim 37 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging.

39. The method of claim 37 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging using <sup>18</sup>fluoro-deoxyglucose.

40. The method of claim 34-39 wherein said tricarboxylate transporter inhibitor is  
10 administered in conjunction with administration of a different anti-cancer compound.

41. The method of claim 34-39 wherein said tricarboxylate transporter inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

42. A method of inducing apoptosis in a cancer cell comprising the step of delivering to  
said cancer cell an amount of a tricarboxylate transporter inhibitor effective to induce  
15 apoptosis in said cell.

43. The method of claim 42 wherein said cancer cell is a cancer cell that is not dependent on endogenously synthesized fatty acid.

44. The method of claim 42-43 wherein said tricarboxylate transporter inhibitor is selected from the group consisting of: 1,2,3-benzenetricarboxylate, isocitrate, malate,  
20 phosphoenolpyruvate, n-butylmalonate, sulphydryl reagents, diethyl pyrocarbonate, 2,3-butanedione, phenylglyoxal, pyridoxal, 5-phosphate dicarboxylates, succinate, malate, oxaloacetate, tricarboxylates isocitrate, tricarballylate and palmitoyl-CoA.

45. A method of treating an individual who has cancer comprising the steps of identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis,

and subsequently administering to said individual a therapeutically effective amount of an tricarboxylate transporter inhibitor.

46. The method of claim 45 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging.

5 47. The method of claim 45 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging using <sup>18</sup>fluoro-deoxyglucose.

48. The method of claim 45-47 wherein said cancer comprises cancer cells that are not dependent on endogenously synthesized fatty acid.

10 49. The method of claim 45-48 wherein said tricarboxylate transporter inhibitor is selected from the group consisting of: 1,2,3-benzenetricarboxylate, isocitrate, malate, phosphoenolpyruvate, n-butylmalonate, sulfhydryl reagents, diethyl pyrocarbonate, 2,3-butanedione, phenylglyoxal, pyridoxal, 5-phosphate dicarboxylates, succinate, malate, oxaloacetate, tricarboxylates isocitrate, tricarballylate and palmitoyl-CoA.

15 50. The method of claim 45-50 wherein said tricarboxylate transporter inhibitor is administered in conjunction with administration of a different anti-cancer compound.

51. The method of claim 45-50 wherein said tricarboxylate transporter inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

20 52. A method of treating an individual who has been identified as having cancer comprising administering to said individual a therapeutically effective amount of a compound which inhibits the expression of ATP citrate lyase or tricarboxylate transporter.

53. The method of claim 54 wherein said cancer is a cancer that comprises cancer cells that have a high rate of aerobic glycolysis.

25 54. A method of identifying a compound with anticancer activity comprising the steps of: identifying a test compound as an inhibitor of ATP citrate lyase or tricarboxylate transporter

and performing an apoptosis assay to determine if said test compound induces apoptosis, wherein a test compound that is an inhibitor of ATP citrate lyase or tricarboxylate transporter and induces apoptosis is a compound with anticancer activity.

55. The method of claim 54 wherein said test compound is identified as an inhibitor of

5 ATP citrate lyase or tricarboxylate transporter by performing an assay to determine if it inhibits activity of ATP citrate lyase or tricarboxylate transporter.

56. The method of claim 54-55 wherein said test compound is an inhibitor of ATP citrate lyase.

57. The method of claim 54-55 wherein said test compound is an inhibitor of

10 tricarboxylate transporter.